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10/732,796	12/10/2003	Shalley K. Gupta	58182US004	5660

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3M INNOVATIVE PROPERTIES COMPANY
PO BOX 33427
ST. PAUL, MN 55133-3427

EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/732,796	GUPTA ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *8,9,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/10/03; 09/17/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Election/Restrictions:

1a. Applicants' election with traverse of Group VI, (claims 1-7 and 10-16), filed on 28 April 2006 is acknowledged.

Applicant's ground of traversal is that the claims of Groups I-X are so interrelated that a search of one group of claims will reveal art to the others. While the nucleotide sequences and polypeptide sequences differ between the identified Groups, all of the polypeptides belong to a closely related family of proteins sharing common functions. Importantly, many sources containing the nucleotide and/or polypeptide sequences recited in the claims of Group VI will also contain the corresponding sequences recited in claims of non-elected Groups. Applicants further submit that searching the invention of Groups I-V and VII-X would require substantial duplication of work on the part of the U.S. Patent and Trademark Office, and this substantial duplication of effort would not be warranted where these claims of different categories are so interrelated. Applicants also discuss the need of separate filling fees for examination of the nonelected claims, as well as the added costs associated with prosecuting two applications and maintaining two patents.

This argument is not found persuasive, because the expression system of Group VI comprises nucleic acid sequences, which differ in structure and function from the nucleic acid sequences that are contained in the expression systems of other groups. For example, the nucleic acid of SEQ ID NO:11 comprises 2753 bases and would not be expected to encode the same polypeptide as nucleic acid of SEQ ID NO:13, which

comprises 5007 bases. According to MPEP § 2434, nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Applicant has not provided any evidence to the contrary, therefore, each nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. §121 and 37 CFR §1.141. Furthermore, contrary to Applicants' argument, searching all the nucleic acids would be burdensome, since a single search would not necessarily reveal art pertinent to all of the nucleic acids. The Examiner takes no issue with the fact that Applicant might incur extra expense due to the filing of independent and patentably distinct inventions, (see MPEP chapter 8 and 35 U.S.C. §121).

The restriction requirement is still deemed proper and is therefore made FINAL.

Status of Claims:

1b. Claims 1-18 are pending, of which claims 1-7 and 10-16, will be searched and examined, in so far as they pertain to an isolated nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:11, encoding the polypeptide of SEQ ID NO:12.

Claims 8-9 and 17-18 are withdrawn from consideration by the Examiner as they are drawn to non-elected invention.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted on 10 December 2003, 17 September 2004, 22 November 2004, 01 December 2005, 08 August 2005 and 09 January 2006 have been received and comply with the provisions of 37 CFR §1.97 and

§1.98. The references have been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Objections:

3. Claims 3 and 4 are objected to because of the following informalities: Claims 3 and 4 recite non-elected sequences. Appropriate correction is required.

Claim rejections-35 USC § 112:

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 3-4 and 13-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an expression system comprising a first the nucleic acid set forth in SEQ ID NO:11, which encodes the polypeptide of SEQ ID NO:12, said expression system further comprising a reporter gene operably linked to a second expression control comprising the interferon alpha promoter, (IFN-α), a vector comprising said expression system, a cultured cell comprising said vector, does not reasonably provide enablement for an expression system comprising a first a degenerate of the nucleic acid of SEQ ID NO:11, or which encodes a polypeptide with one or more conservative amino acid substitutions as recited in claims 3 and 4, or a cultured cell which comprises an expression system that comprises a first nucleic acid, and a reporter gene operably linked to a second expression control comprising a cytokine, which further comprises an expressible IFN-α promoter located on a chromosome on the cultured cell or on an extra-chromosomal vector. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make or use the invention commensurate in scope with these claims.

(Since Applicants elected the nucleic acid of SEQ ID NO:11 encoding the polypeptide of SEQ ID NO:12, the other sequences recited in claims 3 and 4 are not considered). Claim 3 recites ".....or a degenerate variant of ...", while claim 4 recites "....sequences with ***one or more*** conservative amino acid substations...", however, the instant specification discloses only the nucleic acid of SEQ ID NO:11 encoding the polypeptide of SEQ ID NO:12, an expression vector comprising said nucleic acid, (see page 11, lines 23-26). The specification shows that IFN-α is inducible by TLR 6 (SEQ ID NO:11) and that said induction can be measured by luciferase assay, (table 4 on page 14). The instant specification does not disclose other nucleic acids that encode variants of the polypeptide of SEQ ID NO:12 or degenerate variants of EQ ID NO:11 that induce the expression of IFN-α. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to

be conserved over biomolecules of related function upon a significant amount of further research (see Wells, 1990, Biochemistry 29:8509-8517). Regarding claim 13, the specification does not disclose a cultured cell that comprises an expressible nucleic acid sequence that encodes IFN-α linked to a third expression control sequence, in addition to the control sequences recited in claim 1. The specification discloses a cultured host cell which comprises a vector comprising IFN-α and a reporter gene, and a vector comprising the nucleic acid of SEQ ID NO:11. The induction of IFN-α by the polypeptide encoded by the nucleic acid of SEQ ID NO:11, was measured using the luciferace assay, (see pages 12-13). However, the specification does not disclose a cultured cell which comprises a cultured host cell which comprises a vector comprising IFN-α and a reporter gene, and a vector comprising the nucleic acid of SEQ ID NO:11, which further comprises another IFN-α promoter linked to a third expression control. Although, making host cells that are transfected with multiple promoters is routine at the time the claimed invention is filed, the skilled artisan would not know how to use said cell.

The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, due to the large quantity of experimentation necessary to generate the infinite number of

degenerate variants recited in claim 4 and possibly screen same for their ability to encode the desired protein, the lack of direction/guidance presented in the specification regarding which positions would tolerate alterations, in order to provide the desired activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the invention in its full scope as recited in claims 3-4 and 13-16.

Claim Rejections - 35 U.S.C. § 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-7, 10-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 1 is drawn to an expression system which comprises three nucleic acids, however the claim is drafted in such a way that makes it unclear whether these nucleic acids are on the same vector or whether they are on three different vectors. Claim 6, recites a second vector, while claim 7 recites "a vector comprising the expression system of claim 1", therefore, it is unclear how many vectors are involved in making the claimed expression system. Appropriate correction is required.

5b. Claim 4, recites "..... one or more conservative amino acid substitutions.....", however, it is unclear how many amino acids to substitute. The metes and bounds of the claim cannot be ascertained.

5c. Claim 13, recites "...further comprising an expressible nucleic acid sequence that encodes IFN-α operably linked to a third expression control sequence...", however, it is unclear whether the expression system claimed in claim 13, comprises TLR encoding nucleic acid, a reporter gene, a promoter (co-stimulatory, defensin, cytokine, or a chemokine) and an interferon alpha encoding nucleic acid. Clarification is required.

5d. Claims 14 and 16 recite "....wherein the expressible nucleic acid that encodes IFN-α is located a chromosome of the cultured cell, or on an extrachromosomal vector", however, this renders the claim vague, because it is unclear whether the IFN-α encoding nucleic acid referred to in claims 13 and 14, is one that is inserted into a vector or whether it is the naturally occurring one that is found on the host cell. Furthermore, is this IFN-α nucleic acid different than the one cited in claim 2? Appropriate correction is required.

Claims 2-3 and 10-12, 15, are vague and indefinite so far as they depend from claim 1 or claim 14 for the limitations set forth directly above.

Claim rejections-35 USC § 102:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6a. Claim 1 is rejected under 35 U.S.C § 102(b) as being anticipated by Frantz et al (August 1999).

Instant claim 1 is drawn to an expression system (understood as being a cell transformed with vectors comprising the recited nucleic acids), which comprises a first nucleic acid that encodes a toll like receptor, a second nucleic acid sequence which encodes a reporter gene and also operably linked to a second expression control that comprises a cytokine promoter or a co-stimulatory promoter.

Frantz et al disclose an isolated cell that is transfected with a first DNA which encodes a TLR4 receptor, a second DNA which encodes an CD4 protein, and a luciferase reporter gene, (see page 274, column 2 and figure 7 on page 277).

Since the Frantz et al reference discloses a cells transfected with a TLR, a co-stimulatory protein and luciferase reporter gene, the Frantz et al reference anticipates the instant claim 1 in the absence of any evidence to the contrary.

Claim rejections-35 USC § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 4-7, 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frantz et al (08/1999) in view of Venter et al (U.S. 6,900,016, published 05/2005; effective filing date 09/2000).

Claims 1-2, 4-7 and 10-12 are drawn to an expression comprising nucleic acid encoding the polypeptide of SEQ ID NO:12, a reporter gene and IFN-α promoter, vectors comprising said nucleic acids, a mammalian cultured host cell comprising said vectors.

The teaching of Frantz et al are set forth directly above. However, Frantz et al does not teach an expression system that comprises the nucleic acid of SEQ ID NO:11, a reporter gene and an IFN-α promoter.

Venter et al teach an isolated nucleic acid that encodes a polypeptide that shares 100% identity to the polypeptide of SEQ ID NO:12, (see attached sequence comparison A, comparing instant SEQ ID NO:12 to the sequence disclosed by Craig et al).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to establish an expression system comprising nucleic acid encoding the polypeptide of SEQ ID NO:12, with a reporter gene and an inducible promoter, to study the biological activities of the polypeptide of SEQ ID NO:12. At the time the instant invention was filed, it was routine to make isolated host cells comprising nucleic acids encoding specific polypeptides and reporter genes and study

the induction of certain polypeptides as taught by Frantz et al. Therefore, since the nucleic acid encoding the polypeptide of SEQ ID NO:12 is not novel, an expression system comprising said nucleic acid would have been obvious to construct.

One of ordinary skill in the art would have been motivated to combine the teachings of the Frantz et al and Venter et al, because toll like receptor genes play an important role in infection and induction of pro-inflammatory cytokines, and studying these genes is of utmost importance in understanding infection and how to treat it.

Conclusion:

8. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
15 July 2006

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER